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10/691,383	10/21/2003	Valerie Vreeland	02307O-087130US	8387

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
	1652

DATE MAILED: 10/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,383	VREELAND, VALERIE	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 09 August 2004.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 14-36 is/are pending in the application.
 4a) Of the above claim(s) 28-36 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 14-27 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 21 October 2003 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
 Paper No(s)/Mail Date 10/21/03.

4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____.
 5) Notice of Informal Patent Application (PTO-152)
 6) Other: sequence alignment.

The Response to Restriction/Election filed August 9, 2004 is acknowledged. Claims 1-13 were cancelled, and claim 29 was amended by preliminary amendment of Oct 23, 2003. Claims 14-36 are pending and are the subject of this Office Action.

DETAILED ACTION

1. Restriction/Election

The restriction requirement of July 8, 2004 was issued in error, because it did not take into consideration the preliminary amendment of Oct, 23, 2003. The amendment cancelled claims 1-13 and amended claim 29. At the moment the restriction was issued claims 14-36 were pending, thus the restriction reflecting the change in the claims status should be as follows.

- I. Claim 28-36, drawn to a method of recombinant production of vanadium haloperoxidase polypeptide, classified in class 435, subclass 69.1.
- II. Claim 14-24, drawn to vanadium haloperoxidase polypeptide, classified in class 435, subclass 189.
- III. Claim 25-27, drawn to a method for enzymatically halogenating a compound, classified in class 435, subclass 41.

Applicant's election, with traverse, of claims 14-24 drawn to vanadium haloperoxidase polypeptide is acknowledged. The traverse is on the ground that "Groups II [claims 14-24] and III [claims 25-27] are closely related as the claimed method of enzymatic halogenation of Group III requires the use of the recombinant minimal catalytic vanadium haloperoxidase of Group II."

Art Unit: 1652

Upon reconsideration of the restriction requirement the examiner found the Applicants' traverse persuasive. Claims 25-27 are joined to Group II. Thus claims 14-27 are examined on merits. Claims 28-36 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Objections

2.1. Specification

It is noted that the specification lacks a statement listing the relationship of the instant application to earlier filed applications.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

2.2. Claim

Claim 14 is objected to for reciting the term "catalytic helical frame", which is not used in the art. For examination purposes it is assumed that by "catalytic helical frame" Applicants mean the vanadium-binding site that is the catalytic site of the enzyme.

In claim 17 the word "wherein" should be added after the word "the claim".

The second period at the end of claim 18 should be deleted.

3. Rejections

3.1. 35 USC, section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is not clear in recitation the term "catalytic helical frame", which is not used in the art. For examination purposes it is assumed that by "catalytic helical frame" Applicants mean the vanadium-binding site that is the catalytic site of the enzyme.

3.2. 35 USC, section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3.2.1 Lack of written description

Claims 14–15 and 25-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to any

vanadium haloperoxidase or to a vanadium haloperoxidase comprising in position corresponding to position 455 of SEQ ID NO: 2 an Ala, in position corresponding to position 457 a Cys, and at position corresponding to position 525 a Val. Thus, the claims are directed to a large and variable genus of polypeptides comprising vanadium haloperoxidase and a large genus of methods of their use, but the structure of the polypeptides is not sufficiently disclosed in the application. The specification teaches, Fig.3, twelve polypeptides, SEQ ID NO: 2 and its truncated forms, that have the claimed activity. This, however is not sufficient to identify any vanadium peroxidase from any biological source or man-made or an enzyme having in position corresponding to position 455 of SEQ ID NO: 2 an Ala, in position corresponding to position 457 a Cys, and at position corresponding to position 525 a Val.

Given the lack of structural characteristics of additional representative species as encompassed by the claim, Applicants have failed to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention when the application was filed.

3.2.2. *Scope of enablement*

Claims 14-17 and 19-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, its twelve truncated forms presented in Fig. 3 and the method of their use, does not reasonably provide enablement for any vanadium peroxidase polypeptide or an enzyme

having at least 80% identity to SEQ ID NO: 2 or any amino acid sequence having at least 70% amino acid identity of a sequence from residue 435-632 of SEQ ID NO: 2 or an enzyme that comprises the amino acids residues as recited in claim 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of polypeptides encompassed by the scope of the claims; see the above above rejection for lack of written description.

The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any polypeptide, and its metod of use, from any natural or man-made source, wherein the polypeptide:

- (1) is a vanadium haloperoxidase,
- (2) has 80% identity to SEQ ID NO: 2,

- (3) has a sequence that is in at least 70% identical to a sequence from residue 435 to residues 632 of SEQ ID NO: 2, and/or
- (4) comprisesing in position corresponding to position 455 of SEQ ID NO: 2 an Ala, in position corresponding to position 457 a Cys, and at position corresponding to position 525 a Val.

While methods of gene cloning and gene structure manipulations are well known in the relevant art, and skills of the artisans highly developed, no one is able to make polynucleotides and thus encoded polypeptides listed under (1) – (4) above, because the lack of structural characteristics of said polypeptides makes the probability of success in obtaining the claimed invention very low. The only example provided by disclosure is the polypeptide of SEQ ID NO: 2 encoding vanadium haloperoxidase of *Fucus distichus*, or its 11 truncated forms. However, the specification is silent as to how change the structure of disclosed polypeptides so that they had features described under (1)-(4) above and retained the desired activity.

It is concluded that without the further guidance on the part of Applicants in regards of structure of the claimed polypeptides, experimentation left to those in the art is improperly extensive and undue.

3.2. 35 USC section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1652

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Vilter H. [Vanadium dependent haloperoxidases, in Sigel H. Siegel A. (eds.), Metal ions in biological system - vanadium and its role in life, Marcel Dekker, New York 1995, pp. 323-362].

The claims are directed to a polypeptide

- (1) that is a vanadium haloperoxidase,
- (2) has a sequence that is in at least 70% identical to a sequence from residue 435 to residues 632 of SEQ ID NO: 2.

Vilter discloses a vanadium dependent haloperoxidase that in positions 316-513 Comprises a sequence that is 90% identical to amino acid residues 435-632 of SEQ ID NO: 2; see the attached sequence alignment. Thus Vilter teaches polypeptides claimed in claims 14 and 16.

3.3. 35 USC section 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vilter [Vanadium dependent haloperoxidases, in Sigel H. Siegel A. (eds.), Metal ions in biological system - vanadium and its role in life, Marcel Dekker, New York 1995, pp. 323-362] in view of the common knowledge in protein purification as exemplified by Ford et al. (Fusion Tails for the Recovery and Purification of Recombinant Proteins, Protein Expression and Purification, 1991, vol. 2, 95-107).

The claims are directed to the isolated polypeptide having an amino acid sequence having at least 70% amino acid sequence identity to a sequence from residue 435 to residue 632 of SEQ ID NO:2, wherein the polypeptide catalyzes oxidation of o-dianisidine when complexed with a vanadium ion and wherein:

- 1) the polypeptide is immobilized on a solid surface,
- 2) the polypeptide further comprises a cleavable linker sequence,
- 3) cleavable linker sequence is an enterokinase linker sequence,
- 4) the polypeptide further comprises an purification tag, and
- 5) the purification tag comprises a plurality of histidine residues.

Vilter discloses a vanadium dependent haloperoxidase that in positions 316-513 comprises a sequence that is 90% identical to amino acid residues 435-632 of SEQ ID NO: 2; see the attached sequence alignment. Vilter, however does not teach the polypeptide limited as described under 1)-5) above.

It would have been obvious for those having ordinary skill in the art to use the enzyme disclosed by Vilter and modify it as described in claims 20-24 for the purpose of simplifying its purification. Ford et al. teach the modifications described under 1) – 5);

Art Unit: 1652

see the abstract and the body of the article. Ford et al. also teach the enterokinase as a cleavable enzyme (page 102, left column, third line from the bottom).

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole *prima facie* obvious.

Claims 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vilter [Vanadium dependent haloperoxidases, in Sigel H. Siegel A. (eds.), Metal ions in biological system - vanadium and its role in life, Marcel Dekker, New York 1995, pp. 323-362] in view of the common knowledge in biochemistry.

The claims are directed to the method for enzymatically halogenating a compound by any vanadium haloperoxidase or the vanadium haloperoxidase that comprises a sequence that is in at least 70% identical to a sequence from residue 435 to residues 632 of SEQ ID NO: 2.

Vilter discloses a vanadium dependent haloperoxidase that in positions 316-513 comprises a sequence that is 90% identical to amino acid residues 435-632 of SEQ ID NO: 2; see the attached sequence alignment. Vilter, however does not teach the use of the disclosed haloperoxidase for enzymatically halogenating/oxidizing a compound. It would have been obvious for those having ordinary skill in the art to use the enzyme disclosed by Vilter for halogenating/oxidizing a compound, because the use is in accordance with the enzymatic activity of the enzyme.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole *prima facie* obvious.

4. Conclusion

No claim is in condition for allowance, however the claim contain allowable subject matter. The following is the examiner's reasons for indicating allowable subject matter. Applicants disclosed a novel bromoperoxidase form the species *Fucus distichus* and its truncated form. Said truncated form of bromoperoxidase is a fragment consisting of residues 435-632 of the full-length enzyme of SEQ ID NO: 2. The bromoperoxidase of SEQ ID NO: 2 as well as its truncated form consisting of amino acids residues 441-676 are disclosed in the US Patent 6,232,457, issued to Valerie Vreeland et al. on the application 09/151,189 of which the instant application is continuation in part, as well as in the US Patent 6,656,715, issued on application 09/596,794 of which the instant application is a divisional.

The bromoperoxidase set forth by SEQ ID NO:2 and a bromoperoxidase having the sequence residues 435-632 of SEQ ID NO: 2 are free of prior art. The latter invention is also non-obvious, because one skilled in the art who has in his hand the full length sequence of SEQ ID NO: 2 cannot predict that the truncated sequence consisting of amino acids 435-632 retains the bromoperoxidase activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Małgorzata A. Walicka, Ph.D., whose telephone number is (571) 272-0944 and the right fax number is (571) 273-0944. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. EST.

Art Unit: 1652

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (571) 272-0928. The fax phone number for this Group is (571) 273-0937.

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